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REISSUE INTERFERENCE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 030523/0136
Reissue of U.S. Patent No. 5,639,940

In re patent application of

Garner *et al.*

Examiner: Unassigned

Art Unit: 1632

Serial No. 09/232,488

Filed: January 15, 1999

For: Production of Fibrinogen In Transgenic Animals

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PROTEST UNDER 37 C.F.R. § 1.291

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This protest is filed on behalf of Velander *et al.* ("Velander"), the senior party in Interference No. 104,242 ("the interference") between Velander and Garner *et al.* ("Garner"). The protest is timely by virtue of its submission within two months of an Official Gazette notice, dated March 23, 1999, of the request by Garner *et al.* for a reissue of U.S. Patent No. 5,639,940 ("the '940 patent"). See 1220 O.G. 92 (copy attached). Pursuant to 37 CFR § 1.248, a Certificate of Service is attached, indicating that a copy of this protest is served on Garner *et al.*

Velander urges that Garner's Request for Reissue should be denied on account of Garner's failure to present an error which is correctable by reissue, pursuant to 35 USC § 251. All of the claims in the '940 patent are valid, and new claim 34, which Garner proposes to add to its reissue application, is not patentable.

The following exposition tracks arguments that have been made by both parties during the interference. Velander provides the Examiner with some but not all of the papers filed heretofore in the interference, and directs the Examiner to the interference file for a complete history. Velander lists on form PTO-1449 all the documents submitted in this protest.

I. GARNER'S REQUEST FOR REISSUE SHOULD BE DENIED

A. There Is No Error To Be Corrected

Garner has asserted that claims in the '940 patent are unpatentable because they encompass transgenic animals and methods that rely upon the use of cDNA.[1] According to Garner, transgenic production of fibrinogen, using cDNA, would have been obvious because results so obtained would have been expected in view of results obtained in cell cultures.

Garner purported to calculate the exact amount of fibrinogen (78 μg/ml) that could be expected to be produced in a transgenic mouse extrapolated from cell culture data and compared it to the yield in Velander's '068 and '184 applications (50 μg/ml).[2] Thus, Garner has made a quantitative assessment. It has compared levels of expression of fibrinogen in cell cultures with levels of expression in transgenic animals produced using cDNA encoding fibrinogen. It asserts that one of skill in the art would expect expression levels in cell cultures to be the same as expression levels in transgenics. Garner's main argument has been that because the expression levels levels in transgenics using cDNA appear to be

[1] Garner's Preliminary Motion No. 1 (Paper No. 1).

[2] Declaration of Alan Colman ¶¶ 21, 22 (Paper No. 2); Garner Exhibit 28 (Paper No. 28)

similar to expression levels observed with cell cultures, methods and animals using cDNA to transgenically produce fibrinogen would have been obvious.

Garner's reasoning is faulty. Velander believes Garner's conclusions are based upon a comparison of apples with oranges.

1. Results In Cell Cultures Are Not Predictive Of Results In Transgenics

a. *Cell cultures are very different from transgenics*

Garner has made certain assumptions about the relevance of expression levels observed in cell cultures. Garner's arguments and evidence are unpersuasive, however, because, as of the relevant date[3], the skilled worker simply would not have considered the cell-culture results to be predictive of what might occur in transgenic animals.[4] To the contrary, as of the relevant date, the skilled worker would have appreciated that mammalian cell culture systems were so different from transgenic expression systems that one could not generalize reasonably from the latter to the former.

It was known that mammalian cells used in cultures are ***abnormal*** cells by virtue of their ability to continuously grow in culture; in contrast, mammary glands are ***normal*** tissue living and growing in the body of the animal.[5] Mammalian cell culture systems were known to be controlled systems where nutrients, temperatures and growth rates of cells could be easily manipulated and where expressed products could be obtained by standard recovery methods from

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[3] Garner submitted a declaration by Alan Colman, who, in ¶9, defined "relevant date" as being more than one year prior to February 18, 1994 (Paper No. 2).

[4] Toman Declaration ¶¶10, 11 (Paper No. 3); Hennighausen Declaration ¶¶ 12, 13, 14 (Paper No. 4); Rosen Declaration ¶ 14 (Paper No. 5).

[5] Toman Declaration ¶ 10 (Paper No. 3).

the cell culture media.[6] It was known that, in contrast to a mammalian cell culture, the *in vivo* environment of the mammary gland could not be easily controlled because it is influenced by the animal's metabolism and general health and that transgenically produced products might not be easily recovered from the animal's body fluid, which is more complex than a culture media.[7] Moreover, as of the relevant date, the skilled artisan would have appreciated the fact that expression of a protein in a mammalian cell culture would provide no indication as to whether that same protein would have a deleterious effect on the animal in which the protein was transgenically produced.[8]

b. *Results in cell cultures do not correlate with results in transgenics*

As of the relevant date, there were a number of cell-culture systems for expressing proteins. But the expression levels obtained with cell cultures often did not correlate with subsequent expression levels in transgenic systems.[9] As of the relevant date, for instance, tissue plasminogen activator (tPA) encoded by cDNA had been expressed in cell culture at low levels but at high levels in transgenics.[10] Human erythropoietin has been expressed well in cell culture but poorly transgenically.[11] Therefore, as of the relevant date, the skilled artisan would not have considered an expression level in cell cultures to have been

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[6] *Id.*

[7] *Id.*

[8] Toman Declaration ¶ 10 (Paper No. 3); Hennighausen Declaration ¶ 6 (Paper No. 4); Rosen Declaration ¶ 13 (Paper No. 5)and Yarus *et al, Genetic Engineering* 18: 57-81 (1996) (Paper No. 6); Reddy, *et al., Animal Biotechnology* 2: 15-29 (1991) (Paper No. 7); Tojo *et al. J. Reprod. Develp.* 39: 145-155 (1993) (Paper No. 8).

[9] Hennighausen Declaration ¶¶ 12, 13 (Paper No. 4); Rosen Declaration ¶ 11 (Paper No. 5); Toman Declaration ¶ 10 (Paper No. 3).

[10] Hennighausen Declaration ¶ 13 (Paper No. 4).

[11] Massoud *et al, Ann Zootech* 45: 1-9 (1996) (Paper No. 27)

predictive of the expression levels obtained in transgenics for a given protein. Expression levels in both systems are unpredictable. Contrary to Garner's assertion, one of skill in the art would not have expected Velander to obtain any particular expression levels, given results obtained in cell cultures.

c. *Many uncertainties confronted the skilled worker*

Cell-culture technology was not considered analogous, and in fact is not analogous, to transgenic technology.[12] Moreover, even if one of skill in the art had considered cell-culture results in relation to a transgenics context, there would have been no reasonable basis, as of the relevant date, for an expectation of expressing fully assembled, biocompetent fibrinogen in the mammary gland of a transgenic animal, regardless of whether cDNA or genomic DNA was used. There are several reasons for this:

(i) There were no suitable ***mammary gland epithelial cell*** cultures to use as models of the *in vivo* mammary gland.[13]

(ii) Fibrinogen was one of the most complex proteins for which heterologous expression was attempted.[14]

(iii) Conventional wisdom held that the mammary gland secretory pathway might interfere with proper assembly of the fibrinogen chains because chains might be secreted prior to assembly with the other chains and post-translational modification.[15]

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[12] Toman Declaration ¶ 10 (Paper No. 3); Hennighausen Declaration ¶ 12 (Paper No. 4); Rosen Declaration ¶¶ 11, 13, 14 (Paper No. 5).

[13] Toman Declaration ¶ 12 (Paper No. 3); Hennighausen Declaration ¶ 14 (Paper No. 4); Rosen Declaration ¶ 14 (Paper No. 5).

[14] Toman Declaration ¶ 13 (Paper No. 3); Rosen Declaration ¶¶ 7, 8 (Paper No. 5); Farrell et al., Biochemistry 30: 9414-9420 (1991) (Paper No. 9); Colman Declaration ¶ 13 (Paper No. 2).

[15] Toman Declaration ¶ 13 (Paper No. 3); Hennighausen Declaration ¶¶ 15,18 (Paper No. 4); Rosen Declaration ¶ 13 (Paper No. 5).

(iv) Protocols had to be developed for determining the best way to get the three fibrinogen chains into the embryonic cells.[16]

(v) It was not known whether fibrinogen would deleteriously effect the animal.[17]

(vi) It was not known whether the milk contained proteases that would degrade fibrinogen.[18]

As of the relevant date, nothing in the cell culture art provided guidance on any of these points.

B. Garner Believes That Claims Reciting Genomic DNA Are *Prima Facie* Obvious

In Garner's Opposition to Velander's Preliminary Motion No. 1,[19] Garner asserted that claims directed to transgenic animals and methods that recite genomic DNA are *prima facie* obvious and, hence, are not patentable to Velander. These are the same claims that Garner proposes to prosecute in its reissue application. Garner explains that it has overcome the alleged *prima facie* case of obviousness by showing unexpected results, in the form of one animal that produced 2000μg/ml of fibrinogen, as reported in an article by Prunkard *et al.*[20]

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[16] Toman Declaration ¶ 13 (Paper No. 3); Rosen Declaration ¶ 6 (Paper No. 5).

[17] Toman Declaration ¶¶ 10, 13 (Paper No. 3); Rosen Declaration ¶ 13 (Paper No. 5); Hennighausen Declaration ¶ 6 (Paper No. 4).

[18] Toman Declaration ¶ 13 (Paper No. 3); Hennighausen Declaration ¶¶ 6, 16 (Paper No. 4).

[19] Velander's Preliminary Motion No. 1 (Paper No. 12) requested that genomic claims be added to its application; Garner's Opposition to Velander's Preliminary Motion No. 1 (Paper No. 11) argues that such claims are not patentable to Velander.

[20] Prunkard *et al.*, *Nature Biotechnology* 14: 867-871, 870 (1996) (Paper No. 12)

As previously noted, Velander vigorously disagrees with Garner's assertion that claims reciting genomic DNA are *prima facie* obvious. Moreover, Velander vigorously disagrees that Garner has presented evidence of unexpected results, related to the use of genomic DNA.

1. Expression Levels Of Fibrinogen In Transgenics Are Variable

Evidence shows that ***variable*** results can be obtained using either genomic or cDNA, *i.e.*, that expression levels are sometimes low and sometimes high. Prunkard[21] shows that, in a sample of seven transgenic mice produced using genomic DNA, fibrinogen expression ranged from 30 μg/ml to 2,000 μg/ml. Prunkard also explains that ***only one*** mouse produced 2,000 μg/ml, and that only 1,600 μg/ml of the 2,000 μg actually was assembled and, therefore, biocompetent. The average amount of fibrinogen produced by Prunkard was 580 μg/ml.[22] The evidence also shows that fibrinogen is produced transgenically at varying levels, regardless of the type of DNA used. That is, there can be examples of high and low expression levels, respectively, with cDNA as well as genomic DNA.[23]

2. Expression Levels With cDNA Can Be Higher Than With Genomic DNA

Garner has argued that the use of genomic DNA results in unexpectedly higher yields of biocompetent fibrinogen.[24] This is not true. Aside from the variability of results and the above-noted lack of evidence connecting expression yields with the type of DNA used, Garner also fails to demonstrate that

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[21] Prunkard (1996), *supra,* note 22.

[22] *Id.*

[23] Toman Declaration ¶ 8 (Paper No. 3); Hennighausen Declaration ¶¶ 6, 8, 9 (Paper No. 4); Rosen Declaration ¶ 9 (Paper No. 5).

[24] Garner Preliminary Motion No. 1, page 11 (Paper No. 1).

high yields of fibrinogen are even associated with the use of genomic DNA. In fact, expression levels using cDNA can be much higher than with genomic DNA.

To support its arguments, Garner compares the transgenic expression level of 1600 μg/ml (genomic DNA) reported in Prunkard[25] with 50μg/ml (cDNA) taught in U.S. application Serial No. 08/443,184[26]. This comparison, which compares the best genomic DNA expression with the worst cDNA expression, grossly distorts the truth, which is that both types of DNA randomly yield low and high expression levels. Indeed, Velander could make the equally distorted comparison of the highest expression level found with cDNA (700 μg/ml- Velander Declaration ¶¶ 4, 5) with Garner's lowest yield (30 μg/ml) with genomic DNA. Given the reality of random expression for both types of DNA, there can be no argument of unexpectedly higher expression from genomic DNA.

3. There Is No Nexus Between Expression Levels And The Type Of DNA Used

Garner has failed to establish a nexus between the type of DNA used and resultant expression levels of fibrinogen. As of the relevant date, it was known that many factors influence expression levels in transgenics.[27] Factors that influence expression levels include the species of animal, the site at which the DNA is integrated chromosomally, the "copy number" or number of DNA segments that integrate into the animal's chromosome, the promoter and regulatory sequences used and, with particular regard to fibrinogen, the relative rate at which the various chains are accumulated in the intracellular space of mammary gland

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[25] Prunkard et al., supra. (Paper No. 12).

[26] USSN 08/443,184 is Velander's interfering application.

[27] Toman Declaration ¶¶ 9, 13 (Paper No. 3); Hennighausen Declaration ¶¶ 8,10 (Paper No. 4); Rosen Declaration ¶ 10 (Paper No. 5).

epithelial cells, the stability of the mRNA and protein and the ability of the cell to post-translationally modify and assemble the biologically active protein in the milk.[28] Garner has failed completely to demonstrate that the allegedly high expression level is due to the use of genomic DNA and not due to some other factor or combination of factors, as noted above.

4. Garner's Reissue Claims are Too Broad

Velander doesn't believe that Garner has met its burden of showing unexpected results. Although Garner has made much about how its use of genomic DNA results in unexpected expression levels of fibrinogen and how such levels truly are exceptional, Garner has failed to limit its reissue claims to recite what variables are responsible for the alleged exceptional results. As noted above, many variables influence expression levels, *e.g.*, the species of animal, the site at which DNA is integrated chromosomally, the "copy number" or number of DNA segments that integrate into the animal's chromosome, the promoter and regulatory sequences, and the sequence of DNA encoding the protein to be expressed. Garner's claims fail to recite which of the above elements are responsible for the alleged high results. If Garner seriously believes that its observed level of fibrinogen expression is what renders its claims a non-obvious species over claims reciting cDNA, then such claims should recite the elements responsible for the high results. As Velander has previously emphasized, results in transgenic systems are variable. It is clear that high expression levels are not always associated with the use of genomic DNA. Garner's own work shows expression levels as low as 30μg/ml. Thus, Garner cannot argue that **high** expression levels are an inherent property of its constructs or transgenic systems as claimed in the reissue application. It is Garner's burden to show what elements are responsible for allegedly high results and to limit its claims, accordingly.

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[28] *Id.*

C. Expectation Of Success Was Unrelated To The Type Of DNA Used

Garner also has argued that results with genomic DNA were unexpected because one skilled in the relevant art would have had **a lower** expectation of success, in the transgenics context, with genomic DNA versus cDNA[29]. These arguments contradict Garner's own contention that claims reciting genomic DNA would have been *prima facie* obvious. If the prior art cast doubt upon the potential for successful use of genomic DNA, then necessarily there would have been a "teaching away" from the use of genomic DNA, which in turn would have defeated the notion that using genomic DNA was obvious.

Whatever Garner's "true" position, Velander strongly believes that it would not have been obvious to use genomic DNA to prepare transgenic animals that produce fibrinogen. This position is not contradicted by Garner's proffered evidence,[30] which actually is irrelevant in this context. For instance, Garner relied upon Hurtley *et al.*,[31] which has not relevance because it relates to the natural processes of protein folding and assembly in the cell. Thus, the Hurtley article does not speak to processes in recombinant or transgenic systems.[32] Garner also relies upon an abstract by Prunkard *et al.*[33] for teaching protein over-expression. Yet this abstract fails to establish that over-expression of fibrinogen is caused by the type of DNA employed. In fact, the type of DNA used is not identified as a variable, and the reported over-expression of the fibrinogen could have been an

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[29] Garner's Preliminary Motion No. 1, page 13 (Paper No. 1).

[30] Hurtley *et al., Annu. Rev. Cell Biol.* 5: 277-307 (1989) (Paper No. 13); Prunkard *et al.* (Abstract) *J. Cell Biochem., Suppl.* 17C (1993) (Paper No. 14) and Drohan *et al., Transgenic Research* 3: 355-364 (1994) (Paper No. 15).

[31] Hurtley *et al., Annu. Rev. Cell Biol.* 5: 277-307 (1989) (Paper No. 13)

[32] Hennighausen Declaration ¶ 17 (Paper No. 4).; Rosen Declaration ¶ 17 (Paper No. 5).

[33] Prunkard *et al.* (ABSTRACT) (Paper No. 14).

artifact of the BHK cell system employed, as suggested by the author, and not of the DNA type.[34] The teachings of Drohan *et al.*[35] are not probative because they relate to protein C, which is structurally simpler and otherwise very different from fibrinogen. Protein C requires post translational modification (γ-carboxylation) but it does not require the assemblage of three different chains.[36] In any event, the problems observed with protein C were eliminated by using a different species, *i.e.*, pigs instead of mice.[37]

D. Transgenic Art Didn't Address the Complexity of Fibrinogen

Garner also has argued that as of the relevant date, the skilled worker would have expected to produce biocompetent fibrinogen transgenically because fibrinogen shared important functions with other proteins, such as factor IX, α1-antitrypsin, tPA, protein C, serum albumin and urokinase, that already had been transgenically produced in the milk of mammals.[38] The shortcoming of this argument is that Garner fails to show how these proteins are structurally related. In fact, they are not. Additionally, they are not expressed, assembled, post-translationally modified, or activated in the same way as fibrinogen. Therefore, one would not have assumed that success in transgenically expressing any of these other proteins, which might perform a similar function as fibrinogen, would ensure success with fibrinogen.

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[34] Hennighausen Declaration ¶ 17 (Paper No. 4); Rosen Declaration ¶ 17 (Paper No. 5).

[35] Drohan *et al., supra* (Paper No. 15)

[36] Hennighausen Declaration ¶ 18 (Paper No. 4); Rosen Declaration ¶ 18 (Paper No. 5); Toman Declaration ¶ 14 (Paper No. 3).

[37] Toman Declaration ¶ 14 (Paper No. 3), Velander *et al., PNAS USA* 89: 12003-12007 (1992) (Paper No. 16).

[38] Garner's Reply in Support of Garner's Preliminary Motion 1, pp. 3-5. (Paper No. 28).

Garner also looks to generalize between the transgenic expression of fibrinogen and that of multimeric proteins such as FSH (not a blood protein) and protein C. Garner admits, however, that protein C is expressed from a single primary gene product[39], whereas the six chains of fibrinogen are encoded by three separate DNAs. Velander agrees that that FSH is expressed from separate DNAs, but this protein is much less complex than fibrinogen, as has been attested to by Dr. Rosen, the scientist who performed this work.[40]

Pursuant to Garner's present logic, no claims directed to transgenic expression of a protein would ever be allowable, if transgenic expression levels were the same as expression levels observed for the same protein in cell culture, regardless of the complexity of the protein or its mode or site of expression. This is a clear departure from Garner's prior position with regard to the patentability of claims directed to the transgenic production of fibrinogen. During the prosecution of the '940 patent, Garner argued that

> ...fibrinogen is a structurally complex molecule requiring extensive processing and assembly for biological activity, making Applicants' invention a significant and unexpected achievement. Biologically active fibrinogen is a hexameric molecule, making its production in transgenic animals unprecedented. Given the results of the experiments of Roy et al. and others using cultured eukaryotic cells, on[e] could not have predicted Applicants success in producing useful amounts of biologically active, transgenic fibrinogen.[41]

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[39] Second Declaration of Alan Colman, ¶ 9 (Paper No. 29); Declaration of Richard F. Lathe ¶ 8 (Paper No. 30).

[40] Rosen Declaration ¶ 7 (Paper No. 5).

[41] Garner Amendment filed on May 8, 1995.

Velander agrees with Garner's previous position, quoted above. The expression of any level of fully assembled, ***biologically active*** fibrinogen was an unexpected achievement. This was so ***regardless of the type of DNA*** that was used. The successes in expressing fibrinogen in cell culture and the successes in transgenically producing other blood proteins amounted to an invitation to experiment, not a prima facie case of obviousness.

* * *

For the above reasons, Garner has not shown that Garner's claims 1-33 are not patentable and that the reissue application cures any error.

II. Claim 34 Is Directed To Unpatentable Subject Matter

Garner asserts that the '940 patent claims less than what Garner is entitled to because it fails to claim a set of DNA segments. Garner proposes to cure this error by adding claim 34, which is as follows:

> *A set of DNA sequences comprising:*
> *a first DNA segment encoding a secretion signal operably linked to a heterologous fibrinogen Aα chain, the DNA segment comprising genomic DNA encoding the Aα chain;*
> *a second DNA segment encoding a secretion signal operably linked to a heterologous fibrinogen Bβ chain, the DNA segment comprising genomic DNA encoding the Bβ chain; and*
> *a third DNA segment encoding a secretion signal operably linked to a heterologous fibrinogen γ chain, the DNA segment comprising genomic DNA encoding the γ chain, wherein each chain is from the same species, and wherein each of said first, second and third segments is operably linked to additional DNA segments required for its expression in the mammary gland of a host female mammal.*

Failure to claim the above recited subject matter in the '940 patent is no error because the subject matter of claim 34 would have been *prima facie*

obvious to the skilled artisan as of the relevant date. The DNA sequences encoding each of the Aα, Bß and γ chains of fibrinogen (cDNA and genomic DNA) were known and published prior to the relevant date,[42] as were the "additional DNA segments required for its expression in the mammary gland of a host female mammal."

In this regard, Velander directs the examiner's attention to Pittius *et al. Proc. Natl. Acad. Sci. (USA)* 85: 5874 (1988),[43] (WAP promoter with gene for tPA); Simons *et al., Biotechnology* 6: 179 (1988),[44] or Clark *et al., Biotechnology* 7:487 (1989)[45] (BLG promoter for use with Factor IX and human α anti-trypsin); U.S. Patent No. 5,304,489,[46] (casein promoter with any protein); World Patent No. 90/05188,[47] (BLG promoter for use with Factor IX, Factor VIII and human α anti-trypsin); and U.S. Patent No. 5,366,894,[48] (BLG vector for expressing any protein). Farrell *et al., Biochemistry* 30: 9414-9429 (1991),[49] which is prior to the relevant date, discloses mammalian cell culture expression vectors containing each of the Aα,Bβ, and γ DNA sequences under the control of cell promoters, such as an SV-40 early promoter and a metallothionein promoter. Thus, all of the elements of claim 34 were known and available to the skilled artisan and the art suggested their combination. Additionally, one of skill in the art would have expected that one could combine the DNA with the regulatory sequences

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[42] Colman Declaration ¶¶ 14, 15 (Paper No. 2); Rosen Declaration ¶ 18 (Paper No. 5).

[43] Paper No. 17.

[44] Paper No. 18.

[45] Paper No. 19.

[46] Paper No. 20.

[47] Paper No. 22.

[48] Paper No. 21.

[49] Paper No. 9.

successfully.[50] It necessarily follows that the subject matter of claim 34 is obvious, within the meaning of §103, as of the relevant date. Accordingly, Garner was not entitled to obtain patent protection for such subject matter.

Garner attributes "unexpected properties" to the invention covered by claim 34 and asserts that such properties overcome structural obviousness. However, Garner has provided no evidence of "unexpected properties" over the relevant prior art, which is cited above. This art collectively teaches each element of claim 34 and provides the utility and motivation for combining those collective teachings to arrive at the invention of claim 34. Garner's showing of unexpected results is insufficient for reasons set forth above.

[50] Colman Declaration ¶ 19 (Paper No. 2); Garner's Motion to Correct Inventorship, Material Fact Nos. 7-9 (Paper No. 23); Garner Preliminary Motion No. 2, Material Facts 19 and 20 (Paper No. 24) and Henninghausen, *Protein Expression and Publication* 1: 3-8 (1990) (Paper No. 25).

* * *

In view of the above, Velander respectfully requests the Examiner to deny Garner's request for a reissue application. Garner has failed to set forth an error that should be corrected by reissue. Claims that encompass cDNA are not obvious, Garner has failed to show that claims reciting genomic DNA are patentably distinct over those reciting cDNA and claim 34 is directed to unpatentable subject matter.

Respectfully submitted,

May 21, 1999
Date

Patricia D. Granados
Reg. No. 33,683

FOLEY & LARDNER
3000 K Street, N.W. – Suite 500
Washington, D.C. 20007-05109
Telephone: 202/672-5300

Should any fees be necessary in connection with the filing of this paper the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

USSN 09/232,488

CERTIFICATE OF SERVICE

I, Patricia D. Granados, certify that on the 21st of May,1999, I served on Party Garner *et al.* an original copy of the annexed **PROTEST UNDER 37 C.F.R. § 1.291**, by prepaid overnight delivery via Federal Express to party Garner's attorney of record at the following address:

James F. Haley, Jr.
FISH & NEAVE
1251 Avenue of the Americas
New York, New York 10020-1104

Patricia D. Granados, Reg. No. 33,683
Attorney for Senior Party Velander *et al.*
c/o FOLEY & LARDNER
3000 K St., N.W.
Suite 500
Washington, DC 20007-5109

Patent Number	Serial Number	Filing Date	Issue Date	Granted Date
4,869,078	07/238,412	08/31/88	09/26/89	01/26/99
4,960,381	07/231,653	08/10/88	10/02/90	01/25/99
4,997,325	07/343,529	04/26/89	03/05/91	01/25/99
5,329,087	08/072,091	06/07/93	07/12/94	01/25/99
5,329,718	08/000,682	01/05/93	07/19/94	01/25/99

Reissue Applications Filed

Notice under 37 CFR 1.11(b). The reissue applications listed below are open to inspection by the general public in the indicated Examining Groups and copies may be obtained by paying the fee therefor (37 CFR 1.12(b)).

5,088,108, Re. S.N. 09/222,712, Dec. 29, 1998, Cl. 375/012, CELLULAR DIGITAL MOBILE RADIO SYSTEM AND METHOD OF TRANSMITTING INFORMATION IN A DIGITAL CELLULAR MOBILE RADIO SYSTEM, Jan E. Uddenfeldt, et. al., Owner of Record: *Telefonaktiebolaget LM Ericsson, Stockholm, Sweden,* Attorney or Agent: Steven M. duBois, Ex. Gp.: 2711

5,109,528, Re. S.N. 09/235,456, Jan. 21, 1999, Cl. 455/033, HANDOVER METHOD FOR MOBILE RADIO SYSTEM, Jan E. Uddenfeldt, et. al., Owner of Record: *Telefonaktiebolaget LM Ericsson, Stockholm, Sweden,* Attorney or Agent: Steven M. duBois, Ex. Gp.: 3712

5,109,528, Re. S.N. 09/235,456, Jan. 21, 1998, Cl. 455/033, HANDOVER METHOD FOR MOBILE RADIO SYSTEM, Jan E. Uddenfeldt, et. al., Owner of Record: *Telefonaktiebolaget LM Ericsson, Stockholm, Sweden,* Attorney or Agent: Steven M. duBois, Ex. Gp.: 3712

5,208,762, Re. S.N. 09/232,743, Jan. 15, 1999, Cl. 364/478, AUTOMATED PRESCRIPTION VIAL FILLING SYSTEM, Kenneth A. Charhut, et. al., Owner of Record: *Baxter International Inc., Deerfield, IL,* Attorney or Agent: Robert M. Barrett, Ex. Gp.: 1641

5,219,888, Re. S.N. 09/176,003, Oct. 21, 1998, Cl. 514/560, USE OF RETINOIDS FOR TREATMENT AND PREVENTION OF CORONARY ARTERY DISEASE, Andrew S. Katocs Jr., et. al., Owner of Record: *American Cyanamid Co., Stamford, CT,* Attorney or Agent: Rebecca R. Barrett, Ex. Gp.: 1614

5,271,545, Re. S.N. 09/233,194, Jan. 20, 1999, Cl. 228/043, MUFFLE CONVECTION BRAZING/ANNEALING SYSTEM, Jeffrey W. Boswell, et. al., Owner of Record: *Seco/Warwick of Delaware, Inc., Meadville, Pa.,* Attorney or Agent: Paul T. Bowen, Ex. Gp.: 3611

5,297,097, Re. S.N. 09/095,101, Jun. 10, 1998, Cl. 365/205, LARGE SCALE INTEGRATED CIRCUIT WITH SENSE AMPLIFIER CIRCUITS FOR LOW VOLTAGE OPERATION, Jun Etoh, et. al., Owner of Record: *Hitachi Ltd., Tokyo, Japan,* Attorney or Agent: John R. Mattingly, Ex. Gp.: 2818

5,548,651, Re. S.N. 09/140,413, Aug. 26, 1998, Cl. 381/67, LUER-RECEIVING MEDICAL VALVE AND FLUID TRANSFER METHOD, Lawrence A. Lynn, Owner of Record: *Inventor,* Attorney or Agent: Michelle N. Lester, Ex. Gp.: 2743

5,592,939, Re. S.N. 09/231,854, Jan. 14, 1999, Cl. 128/653, METHOD AND SYSTEM FOR NAVIGATING A CATHETER PROBE, Michael A. Martinelli, Owner of Record: *Medtronic Inc.,* Attorney or Agent: Toby H. Kusmer, Ex. Gp.: 1632

5,593,382, Re. S.N. 09/229,550, Jan. 13, 1999, Cl. 602/018, EXTRICATION CERVICAL COLLAR WITH ADJUSTABLE SUPPORTS, Ronald M. Rudy, Jr., et. al., Owner of Record: *Ambu Inc., Linthicum, Maryland,* Attorney or Agent: Paul Grandinetti, Ex. Gp.: 3733

5,594,081, Re. S.N. 09/229,956, Jan. 14, 1999, Cl. 526/127, CATALYST COMPONENT FOR THE POLYMERIZATION OF ALPHA-OLEFINS AND A PROCESS FOR PREPARING ALPHA-OLEFIN POLYMERS WITH USE OF SAME, Hideshi Uchino, et. al., Owner of Record: *Mitsubishi Chemical Corp., Tokyo-to, Japan,* Attorney or Agent: Richard D. Kelly, Ex. Gp.: 1713

5,595,687, Re. S.N. 09/234,959, Jan. 21, 1999, Cl. 252/312, EMULSION STABILITY, Stuart Raynolds, et. al., Owner of Record: *Thomas Jefferson University, Philadelphia, Pa.,* Attorney or Agent: Robert A. Hodges, Ex. Gp.: 2812

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